

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
9 December 2004 (09.12.2004)

PCT

(10) International Publication Number
WO 2004/106921 A3

(51) International Patent Classification⁷: **G01N 33/50**,
C12N 5/06, C12Q 1/68

(21) International Application Number:
PCT/CA2004/000788

(22) International Filing Date: 27 May 2004 (27.05.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/473,153 27 May 2003 (27.05.2003) US

(71) Applicant (for all designated States except US): **MCGILL
UNIVERSITY** [CA/CA]; 845 Sherbrooke Street West,
Montréal, Québec H3A 2T5 (CA).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **ROSENBERG,**
Lawrence [CA/CA]; 6507, Fern Road, Côte St-Luc,
Québec H4V 1E4 (CA).

(74) Agent: **OGILVY RENAULT**; Suite 1600, 1981 McGill
College Avenue, Montreal, Quebec H3A 2Y3 (CA).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW.

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,
FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

(88) Date of publication of the international search report:
9 June 2005

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: *IN VITRO* PLATFORM FOR SCREENING AGENTS INDUCING ISLET CELL NEOGENESIS

(57) Abstract: The present invention relates to an *in vitro* method for screening agents inducing islet cell neogenesis or duct-to-islet cell transdifferentiation, which comprises the steps of: a) expanding *in vitro* cells of a duct-like structure obtained by inducing cystic formation in cells in or associated with post-natal islets of Langerhans; b) treating said expanded cells of said duct-like structure with an agent screened; and c) determining potency of said agent of inducing islet cell differentiation of said duct-like structure in becoming insulin-producing cells.

WO 2004/106921 A3

INTERNATIONAL SEARCH REPORT

International Application No
PCT/CA2004/000788

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/50 C12N5/06 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, WPI Data, PAJ, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	KORSGREN O ET AL: "IN VITRO SCREENING OF PUTATIVE COMPOUNDS INDUCING FETAL PROCINE PANCREATIC BETA-CELL DIFFERENTIATION: IMPLICATIONS FOR CELL TRANSPLANTATION IN INSULIN-DEPENDENT DIABETES MELLITUS" UPSALA JOURNAL OF MEDICAL SCIENCES, UPSALA MEDICAL SOCIETY, SE, vol. 98, no. 1, 1993, pages 39-52, XP000978995 ISSN: 0300-9734 see the whole document ----- -/--	1-4

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *Z* document member of the same patent family

Date of the actual completion of the international search

17 September 2004

Date of mailing of the international search report

11.02.05

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Grosskopf, R

INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA2004/000788

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	BONNER-WEIR ET AL: "In vitro cultivation of human islets from expanded ductal tissue" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 97, no. 14, 5 July 2000 (2000-07-05), pages 7999-8004, XP002144480 ISSN: 0027-8424 see abstract	1-4
Y	OBERG-WELSH C ET AL: "Effects of certain growth factors on in vitro maturation of rat fetal *islet*-like structures" PANCREAS, RAVEN PRESS, NEW YORK, NY, US, vol. 12, no. 4, 1 May 1996 (1996-05-01), pages 334-339, XP002090017 ISSN: 0885-3177 see para. bridging page 334 and 335	1-4
Y	WO 01/77300 A (RAVEN BIOTECHNOLOGIES INC ; MATHER JENNIE POWELL (US); ROBERTS PENELOP) 18 October 2001 (2001-10-18) see pages 24, line 15 to 32	1-4
A	US 2003/082155 A1 (ZULEWSKI HENRYK ET AL) 1 May 2003 (2003-05-01)	
A	US 5 587 309 A (BEATTIE GILLIAN M ET AL) 24 December 1996 (1996-12-24) see col. 4, lines 14 to 51	
A	US 6 001 647 A (CORNELIUS JANET G ET AL) 14 December 1999 (1999-12-14)	
A	BOUWENS LUC ET AL: "Islet cell neogenesis in the pancreas" VIRCHOWS ARCHIV, vol. 427, no. 6, 1996, pages 553-560, XP008035542 ISSN: 0945-6317	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CA2004/000788

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0177300	A	18-10-2001	US 6436704 B1	20-08-2002
			AU 5759701 A	23-10-2001
			CA 2404313 A1	18-10-2001
			CN 1425061 T	18-06-2003
			EP 1272616 A2	08-01-2003
			JP 2003530102 T	14-10-2003
			WO 0177300 A2	18-10-2001
			US 2002192816 A1	19-12-2002
US 2003082155	A1	01-05-2003	US 2001046489 A1	29-11-2001
			US 2002164307 A1	07-11-2002
			CA 2461861 A1	03-04-2003
			EP 1438418 A2	21-07-2004
			WO 03026584 A2	03-04-2003
			AU 1817301 A	12-06-2001
			CA 2392615 A1	07-06-2001
			CN 1423563 T	11-06-2003
			EP 1257282 A1	20-11-2002
			JP 2003523323 T	05-08-2003
			WO 0139784 A1	07-06-2001
			US 2003031657 A1	13-02-2003
			US 2001024824 A1	27-09-2001
US 5587309	A	24-12-1996	AT 270323 T	15-07-2004
			AU 695390 B2	13-08-1998
			AU 2433695 A	29-11-1995
			CA 2189052 A1	09-11-1995
			DE 69533223 D1	05-08-2004
			EP 0765385 A1	02-04-1997
			JP 10503923 T	14-04-1998
			WO 9529989 A1	09-11-1995
			US 5888705 A	30-03-1999
US 6001647	A	14-12-1999	US 5834308 A	10-11-1998
			AU 739771 B2	18-10-2001
			AU 7468396 A	15-05-1997
			CA 2235509 A1	01-05-1997
			EP 0871455 A1	21-10-1998
			JP 11514877 T	21-12-1999
			WO 9715310 A1	01-05-1997
			US 6703017 B1	09-03-2004
			AU 709165 B2	26-08-1999
			AU 2369595 A	29-11-1995
			CA 2188648 A1	09-11-1995
			EP 0758376 A1	19-02-1997
			JP 9512440 T	16-12-1997
			WO 9529988 A1	09-11-1995

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2004/000788

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of Item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-4

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-4

An in vitro method for screening agents inducing islet cell neogenesis or duct-to-islet cell transdifferentiation, which comprises the steps of

- (a) expanding in vitro cells of a duct-like structure obtained by inducing cystic formation in cells in or associated with post-natal islets of Langerhans;
- (b) treating said expanded cells of said duct-like structure with an agent being screened; and
- (c) determining potency of said agent of inducing islet cell differentiation of said duct-like structure in becoming insulin-producing cells

2. claims: 5-7

A kit comprising

- (a) a solid matrix for 3-D culture cells;
- (b) a culture medium supplemented

3. claims: 8-12

An islet cell culture, which comprises insulin-producing islet cells in a suitable culture medium, wherein said islet cells are characterised and a method for evaluating biological effects of agents on said cells
